UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/845,020	04/27/2001	Douglas A. Treco	50010/017003	1549

35093 7590 09/23/2003

CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER
VOGEL, NANCY T

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 09/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/845,020	TRECO ET AL.	
	Examiner	Art Unit	
	Nancy Vogel	1636	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 35-50 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 35-50 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 27 April 2001 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 35-50 are pending in the case. Receipt of preliminary amendment on 4/27/01 is acknowledged. Receipt of an Information Disclosure statement on 6/25/01 is acknowledged. Receipt of a letter re: fee, and sequence listing, on 8/8/01 is acknowledged. Receipt of a raw sequence listing on 10/23/01 is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The following factors have been considered in formulating this rejection (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction of guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

The nature of the invention. The claimed invention is drawn to a gene therapy method, in particular, an ex vivo method, whereby it is contemplated that modified cells are in some manner transplanted or implanted into the animal. It is also noted that animals as subjects includes human patients.

The amount of direction or guidance presented in the specification, and the presence or absence of working examples. Applicants present general guidance in the form of teachings that the appropriate level of G-CSF expression be selected for the patient, without specific information about such levels and how to be certain they are maintained during treatment. A very large list of possible cell types to be modified and implanted is set forth at page 28. However, it stands to reason that different cell types, especially laboratory strains, would have very different potentials for expression of a recombinant polypeptide, e.g. G-CSF. No teachings to circumvent extra experimentation to adapt the selected cell type to the claimed methods is set forth. Applicants give essentially no guidance for the selection of protocols for injection or direct implantation of modified cells, including specific information regarding what levels of expression and protocols to use for any particular G-CSF-related disease. No teaching of actual amelioration of a disease state was set forth.

The state of the prior art. Orkin et al. ("Report and Recommendations of the Panel to Assess the NIH Investment in Research on Gene Therapy", National Institutes of Health (1995)) sets forth, as summarized at the first and second pages, item 3, that the Panel to Assess the NIH investment in Research on Gene Therapy (the "Panel") found that "clinical efficacy has not been definitively demonstrated at [that] time in any

gene therapy protocol", that "[s]ignificant problems remain in all basic aspects of gene therapy", and that available vectors, and understanding in the art of the interactions between said vectors with the host, are inadequate.

Predictability or unpredictability of the art. Orkin et al. teaches that the Panel found that, at item 5, "[I]t is not always possible to extrapolate directly from animal experiments to human studies, indeed, in some cases...animal models do not satisfactorily mimic the major manifestations of the corresponding human disease." Clearly, prediction of the success in the patient of a gene therapy protocol, where still only on paper, is not recognized in the art as reliable. At the ninth page, under "Expression of transferred gene", it taught that the expression level of genes after transfer into cells in vivo was problematic and poorly understood at the time of filing. Further, the editorial from Nature Biotechnology (Nature Biotechnology, Vol. 15, p. 815, 1997) hereinafter "the editorial") and Verma (Nature Vol. 389, pp. 239-242, (1997)) demonstrate that gene therapy methods were not routine in the prior art. The editorial comments directly on the impact that Orkin et al. had on the field of gene therapy, showing that, while gene therapy is expected to be a useable field of therapy eventually, it clearly could not have been viewed as routine or even occasionally successful as of September 1997. Verma et al. establishes clearly, e.g. at page 242, final concluding paragraph, that gene therapy was not routine in the medical field a of September 1997.

The quantity of experimentation. It is clear from Orkin et al., from the findings and recommendations of the Panel, and from the editorial and Verma et al., that a very large

amount of experimentation of a complex nature will be required to develop any gene therapy protocol to the point of efficacy.

Were the skilled practitioner in the art to have attempted to practice the claimed methods, which are drawn to ex vivo embodiments, i.e. gene therapy, said practitioner would have turned first to the specification for guidance in selecting implantation protocols., treatment regimens and other factors which may bear upon the success of such treatment. However, as set forth supra, such guidance in the specification is limited in nature, and is insufficient with respect to prediction of proper levels of expression. Said practitioner then would have turned to the prior art, including that generally recited by the specification, to obtain detailed guidance for practice o the claimed methods. However, as set forth supra, the prior art doe not recognize any clearly successful gene therapeutic methods. Thus, the skilled practitioner would not have been able to find the necessary guidance n the prior art. Finally, said practitioner would have been forced to turn to empirical experimentation to determine implantation protocols, treatment regimens and other factors, required for successful practice of a gene therapy method. However, as set forth supra, the amount of experimentation recognized by the art as required for the development o a successful gene therapy protocol is very large, with the assay for determining dosages set forth in the specification employing mere trial-an-error. Further as set forth supra, the field of gene therapy is unpredictable. As large amount of experimentation in an unpredictable art with little or no available guidance is clearly undue experimentation.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy Vogel whose telephone number is (703) 308-4548. The examiner can normally be reached on 7:30 - 4:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

***

TERRY MCKELVEY
PRIMARY EXAMINER